

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listing, of claims in the application:

Claim 1 (withdrawn): A recombinant host cell of the suborder *Cystobacterineae* containing a recombinant expression vector that encodes a heterologous polyketide synthase (PKS) gene and produces a polyketide synthesized by a PKS enzyme encoded on said vector.

Claim 2 (withdrawn): The host cell of Claim 1 that is selected from the family *Myxococcaceae*.

Claim 3 (withdrawn): The host cell of Claim 1 that is selected from the family *Cystobacteraceae*.

Claim 4 (withdrawn): The host cell of Claim 2 that is selected from a genus selected from the group consisting of *Angiococcus*, *Myxococcus*, and *Corallococcus*.

Claim 5 (withdrawn): The host cell of Claim 3 that is selected from a genus selected from the group consisting of *Cystobacter*, *Melittangium*, *Stigmatella*, and *Archangium*.

Claim 6 (withdrawn): The host cell of Claim 4 that is selected from the genus *Myxococcus*.

Claim 7 (withdrawn): The host cell of Claim 5 that is selected from the genus *Stigmatella*.

Claim 8 (withdrawn): The host cell of Claim 6 that is selected from the group consisting of *M. stipitatus*, *M. fulvus*, *M. xanthus*, and *M. virescens*.

Claim 9 (withdrawn): The host cell of Claim 7 that is selected from the group consisting of *S. erecta*, and *S. aurantiaca*.

Claim 10 (withdrawn): The host cell of Claim 8 that is *Myxococcus xanthus*.

Claim 11 (withdrawn): A method for producing a polyketide in a host cell of the suborder *Cystobacterineae*, which polyketide is not naturally produced in said host cell, said method comprising culturing a host cell of Claim 1 under conditions such that a PKS gene encoded on the vector is expressed and said polyketide is produced.

Claim 12 (withdrawn): The recombinant host cell of Claim 1 that produces epothilone or an epothilone derivative.

Claim 13 (withdrawn): The host cell of Claim 10 that produces epothilone or an epothilone derivative.

Claim 14 (withdrawn): The host cell of Claim 13 that produces epothilones A, B, C, and D.

Claim 15 (withdrawn): The host cell of Claim 14 that is *Myxococcus xanthus* K111-32.25.

Claim 16 (withdrawn): The host cell of Claim 14 that produces epothilones A and B as major products and epothilones C and D as minor products.

Claim 17 (withdrawn): The host cell of Claim 13 that produces epothilones C and D as major products.

Claim 18 (withdrawn): The host cell of Claim 17 that either does not contain an *epoK* gene or does not express a fully functional *epoK* gene product.

Claim 19 (withdrawn): The host cell of Claim 18 that is *Myxococcus xanthus* K111-40.1.

Claim 20 (withdrawn): The host cell of Claim 18 that is *Myxococcus xanthus* K111-72.4.4.

Claim 21 (withdrawn): The host cell of Claim 13 that contains an epothilone PKS gene in which a coding sequence for a module of said PKS has been altered by mutation, deletion, or replacement.

Claim 22 (withdrawn): The host cell of Claim 21, wherein said module is extender module

Claim 23 (withdrawn): The host cell of Claim 22, wherein said module lacks a functional ketoreductase domain and produces a 9-keto epothilone.

Claim 24 (withdrawn): The host cell of Claim 21, wherein said module is extender module

Claim 25 (withdrawn): The host cell of Claim 24, wherein said module 5 lacks a functional dehydratase domain and produces a 13-hydroxy epothilone.

Claim 26 (withdrawn): The host cell of Claim 21, wherein said module is extender module

Claim 27 (withdrawn): The host cell of Claim 26, wherein said module lacks a functional ketoreductase domain and produces a 13-keto epothilone.

Claim 28 (withdrawn): The host cell of Claim 21, wherein said module is extender module 2, the coding sequence for the ketosynthase domain has been altered by mutation to change an active site cysteine to another amino acid, and which host cell must be provided a diketide equivalent compound to produce an epothilone or epothilone derivative.

Claim 29 (withdrawn): The host cell of Claim 28 that is *Myxococcus xanthus* strain K90-132.1.1.2.

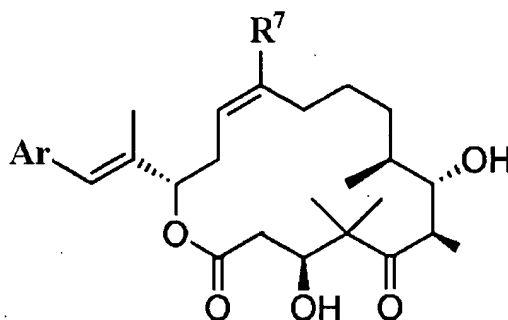
Claim 30 (withdrawn): The host cell of Claim 21, wherein said module is extender module

Claim 31 (withdrawn): The host cell of Claim 30, wherein said module has been changed so that it binds an amino acid other than cysteine.

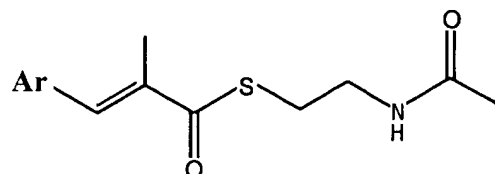
Claim 32 (withdrawn): The host cell of Claim 21, wherein said module is a loading module.

Claim 33 (withdrawn): The host cell of Claim 32, wherein said module has been replaced with a module that binds an amino acid.

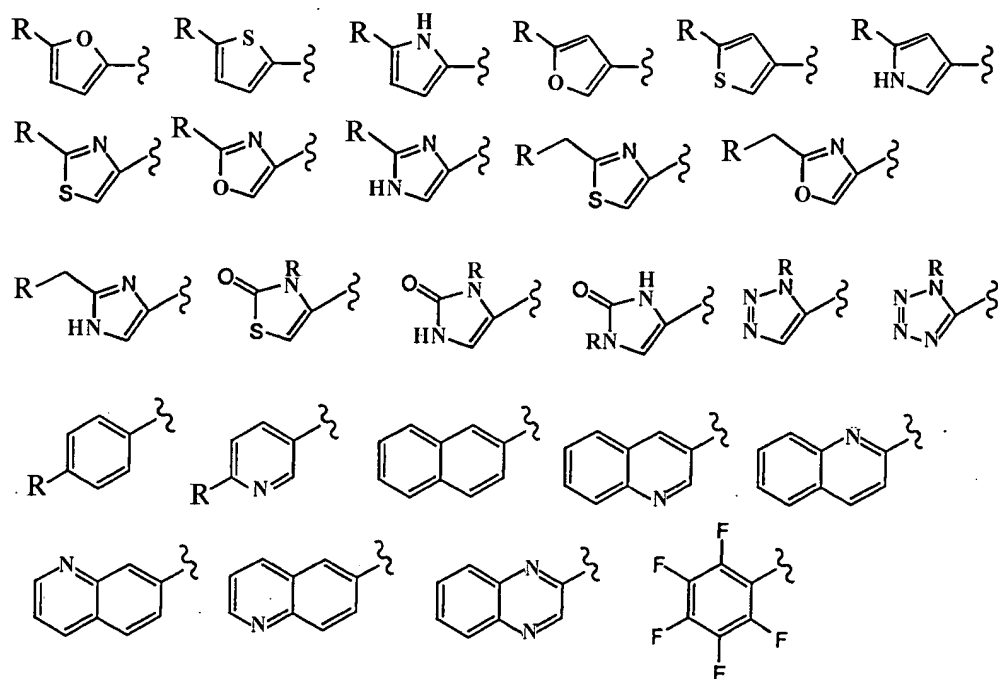
Claim 34 (withdrawn): An epothilone derivative of the formula



produced by culturing said host cell of Claim 28 with a diketide equivalent compound of the formula



where  $R^7$  is hydrogen or methyl and  $Ar$  is aryl is selected from the group consisting of



where R is hydrogen, hydroxy, halogen, amino, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> hydroxyalkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, and C<sub>1</sub>-C<sub>5</sub> aminoalkyl.

Claim 35 (withdrawn): The host cell of Claim 1 that further comprises a heterologous gene that encodes for an enzyme selected from the group consisting of an enzyme that transports a compound into said cell that is utilized in biosynthesis of the polyketide, an enzyme that synthesizes a compound utilized in biosynthesis of the polyketide, and an enzyme that phosphopantetheinylates a PKS.

Claim 36 (withdrawn): The host cell of Claim 35, wherein said enzyme is MatB.

Claim 37 (withdrawn): The host cell of Claim 35, wherein said enzyme is MatC.

Claim 38 (withdrawn): The host cell of Claim 35, wherein said enzyme is MtaA.

Claim 39 (withdrawn): The host cell of Claim 13, wherein said epothilone or epothilone derivative is produced by a PKS gene under the control of a promoter selected from the group

consisting of a promoter from an *S. cellulosum* epothilone PKS gene, a promoter from a myxothiazol biosynthesis gene, a promoter from a TA biosynthesis gene, a *pilA* promoter, a promoter from a kanamycin resistance conferring gene, and a *So ce90* promoter.

Claim 40 - 41 (cancelled):

Claim 42 (withdrawn): Crystalline epothilone D.

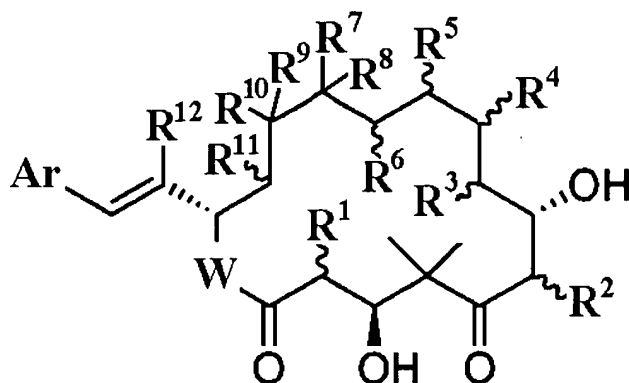
Claim 43 (withdrawn): A method for fermentation of a *Myxococcus* host cell, which method comprises culturing said cell in liquid medium comprising a fatty acid or oil as a carbon source.

Claim 44 (withdrawn): The method of Claim 43, wherein said fermentation is a fed-batch fermentation.

Claim 45 (withdrawn): The method of Claim 43, wherein said *Myxococcus* host cell produces an epothilone or an epothilone derivative.

Claim 46 (withdrawn): The method of Claim 45, wherein said host cell produces an epothilone derivative that contains an oxazole instead of a thiazole, and said liquid medium comprises L-serine.

Claim 47 (withdrawn): A isolated compound of the formula



wherein:

- $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^{11}$ , and  $R^{12}$  are each independently hydrogen, methyl or ethyl;  
 $R^4$ ,  $R^6$  and  $R^9$  are each independently hydrogen, hydroxyl, or oxo; alternatively  $R^5$  and  $R^6$  together form a carbon carbon double bond;  
 $R^7$  is hydrogen, methyl, or ethyl;  
 $R^8$  and  $R^{10}$  are both hydrogen or together form a carbon carbon double bond or an epoxide;  
 Ar is aryl; and,  
 W is O or  $NR^{13}$  where  $R^{13}$  is hydrogen,  $C_1$ - $C_{10}$  aliphatic, aryl or alkylaryl.

Claims 48- 65 (Cancelled):

66. (New): A method for isolating epothilone D from an epothilone D-producing *Myxococcus xanthus* cell, said method comprising
- (a) culturing said cell in the presence of methyl oleate;
  - (b) culturing said cell in the presence of XAD resin; and
  - (c) eluting said epothilone from said XAD resin, thereby producing an eluate comprising epothilone.
67. (New): The method of claim 66 further comprising a crystallization step in which epothilone D is crystallized from a binary solvent system in which water is the forcing solvent.
68. (New): The method of claim 67 wherein the binary solvent system is ethanol and water.

69. (New): A method for obtaining epothilone D from an epothilone D-producing cell, said method comprising

- (a) culturing said cell in the presence of XAD resin;
- (b) eluting said epothilone from said XAD resin to obtain isolated epothilone D;
- (c) subjecting said isolated epothilone D to further chromatography; and
- (d) crystallizing said isolated epothilone D from a binary solvent system in which water is the forcing solvent, thereby obtaining epothilone D that is more than 95% purified.

70. (New): A method for obtaining epothilone D in crystalline form comprising crystallizing epothilone D from a binary solvent system in which water is the forcing solvent.

71. (New): The method of claim 70 wherein the binary solvent system is ethanol and water.

72. (New): The method of claim 71 wherein the epothilone D in crystalline form is more than 95% purified.